Original Articles

Euroroundup

Public health concerns in bat rabies across Europe

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Rabies due to two independent and different genotypes of lyssaviruses - *European bat* lyssaviruses (EBLV) type 1 and type 2 - is present in many European countries. Infection is usually seen in bats, the primary reservoirs of the viruses but a few spillover infections have been seen in three other species: stone martens, sheep and humans. Spillover infections (with the exception of the two human cases) were EBLV-1 only. No EBLV-2 spillover cases have been reported in terrestrial animals.
The disease is fatal in humans and has been described in Europe following a bat bite. We have studied in the available literature EBLV rabies cases across Europe in bats and humans, and have also carried out an analysis of recommendations for rabies prevention and treatments in humans. Rabies pre-exposure vaccination and post-exposure treatment is recommended for occupationally exposed persons. Some European countries have already adopted recommendations through specific protocols. Treatment of international travellers after bat bites is also recommended. The promoting of research programmes on bat rabies in Europe is underway. Bats are listed as protected species across Europe.

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Key words: bats, health education, lyssaviruses, mandatory testing, public health practice, rabies, vaccination

Introduction

Over one thousand species of bats are known worldwide. In recent years, evidence has suggested that they are like most animals reservoirs or biological and accidental vectors for different kinds of micro-organisms including lyssaviruses, West Nile virus, Venezuelan equine encephalomyelitis virus, Hendra virus, Menangle virus, and *Histoplasma capsulatum* [1,2]. Nipah, Menangle and Hendra viruses have all been isolated from bats. Rabies is a notifiable disease in European countries both within and outside the European Union.

Bat rabies has been laboratory confirmed in different parts of the world, and is a public health concern [3]. Much literature has been published on this subject, mostly in the Americas. In Europe, over 30 species of bats have been recognised [4]. All are protected under the *Agreement on the Conservation of Population of European bats* [5]. It has been demonstrated that some but not all bat species carry the viruses. EBLVs are host-specific to specific bat species. Although the common serotine bat (*Eptesicus serotinus*) is mainly affected by EBLV1, different mouse-eared bats (*Myotis spp.*) are more affected by EBLV2.

Most human cases worldwide result from a dog bite or other contact with terrestrial mammals. Bat rabies in humans in Europe is very rare, but in some other parts of the world e.g. USA and Brazil is more frequently recognized. Bat bites may go unrecognised, while bites from terrestrial carnivores are usually noticed. Large outbreaks of bat rabies have been observed in South America in humans and in livestock, associated with bites of the vampire bat (*Desmodus rotundus*), a species only seen in Central and South America [6].

The *Lyssavirus* genus, within the *Rhabdoviridae* family, is subdivided into seven genotypes based on RNA sequencing [7-9]:

- genotype 1 - classical rabies virus, worldwide
- genotype 2 - Lagos bat virus, Africa
- genotype 3 - Mokola virus, Africa
- genotype 4 - Duvenhage virus, Africa
- genotype 5 - European bat lyssavirus 1 (EBLV-1), Europe
- genotype 6 - European bat lyssavirus 2 (EBLV-2), Europe
- genotype 7 - Australian bat lyssavirus, Australia.

Rabies in bats in Europe are caused by two independent lyssavirus infections, distinct from rabies infections in foxes, dogs, cats, cattle and other terrestrial animals. Classic rabies virus strains associated with terrestrial animals are from genotype 1.

This paper deals with bat rabies across Europe, and rabies pre-exposure vaccination and post-exposure treatment in humans.

Lyssaviruses and rabies in European bat species

In Europe, bats are infected by two different lyssavirus genotypes, genotype 5 (EBLV-type 1) and genotype 6 (EBLV type-2). Both are related to the classical rabies virus, although EBLV2 is closer to genotype 1 than EBLV1 [3,10]. EBLV-1 and EBLV-2 have been subdivided into two phylogenetic lineages, EBLV-1a and EBLV-1b and EBLV-2a and EBLV-2b.

A different bat lyssavirus, named Aravan was recently isolated from a lesser mouse-eared bat, *Myotis blythii* [11] and a new lyssavirus, *West Caucasian bat virus*, was isolated in *Miniopterus schreibersii* in 2002 [12]. Their position within *Lyssavirus* genus is still being studied. Modern methods based on phylogenetic relationships were used, comparing nucleotide sequences of the nucleoprotein gene and the amino acid sequence to find the phylogenetic tree showing genetic relationships between different lyssaviruses.

Infection with EBLV has occurred in Europe in several bat species [13-16]. Rabies in bats has been reported from the Netherlands, Germany, France, Spain, Switzerland, Hungary, Poland, Denmark, Lithuania, the Russian Federation, Ukraine, Slovakia, Finland, and the United Kingdom.

In France, 14 cases of bats rabies caused by EBLV-1 have been diagnosed from 1989 to 2002, all in serotine bats (*Eptesicus serotinus*) [13]. EBLV-1a strains have been distributed in northeastern France and EBLV-1b strains in the northwest. European bat lyssavirus type 1, EBLV-1 (genotype 5), is enzootic in the insectivorous bat populations in Germany. In 2001, a single stone marten (*Martes foina*) was infected with EBLV-1a [16]. No clinical signs were observed as the animal was found dead. EBLV-1 has been identified in Spain17]. The results came from serology and RT-PCR. EBLV-2a has been isolated in the United Kingdom [14]. The geographic distribution of infected bat species across other European countries according to laboratory determined genotypes of lyssaviruses has been described by different authors [18-21]. EBLV-1 has been found in *E. serotinus* in Denmark, the Netherlands, Poland, and Switzerland.

Host restriction of EBLV

Bats are the primary reservoir of EBLV viruses, but natural infections have occurred in at least three other species. In very rare

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circumstances, infections with the same lyssaviruses have been identified in a stone marten (1 case), sheep (2 cases) and humans [22]. To date, only three cases of rabies in humans have been reported and confirmed: one case was infected with EBLV-1 and two with EBLV-2 [14] [Table 1].

Table 1

Human rabies of bat origin – Europe

Year	Infected by	Country	Age of patients	Patient	Site of bite
1985	EBLV-1	Ukraine	11	Girl	Lower lip
1985	EBLV-2	Finland*	30	Bat researcher	Multiple bites
2002	EBLV-2	Scotland	56	Wildlife biologist	Probably on the fingers

* This bat researcher had been mainly working on bats in Finland and Switzerland, but had also been working in Asia

Protection of humans

According to recommendations from the World Health Organization (WHO) and other institutions [3,21,23], post-exposure treatment after a bat bite is advised. Anyone exposed to bats should be vaccinated preventively against rabies. Post-exposure vaccination and treatment are recommended after a bite or after exposure to bats [Tables 2 and 3].

Table 2

Bats and recommendations for rabies protection in Europe

Pre-exposure rabies vaccination	Post-exposure rabies treatment
All bat handlers and people who work with bats should receive pre-exposure rabies vaccination	After a bite of EBLV positive bat
Persons who frequently come in contact with bats in their spare time (for instance, cavers or amateur bat handlers)	Post-exposure prophylaxis should be considered when contact between a human and bat has occurred unless the exposed person can rule out a bite, scratch or exposure to a mucous membrane Travellers bitten by a bat: • Arrived from bat rabies infected countries that report bat bites • Arrived from countries where epidemiological data on bat rabies are missing

Sources:

1. WHO. Introduction of an information leaflet on bat rabies and bat conservation. Rabies Bulletin Europe 2003; 27(4): 5-7

2. CDC. International Notes Bat Rabies - Europe. MMWR 1986; 35(26): 430-2

Humans bitten by a bat suspected to be infected with lyssavirus receive post-exposure prophylaxis. In previously unvaccinated persons this consists of an immediate injection of vaccine (days 0, 3, 7, 14, and 28) with additional anti-rabies immunoglobulin (20 IU/kg of body weight). Unvaccinated persons should receive an immediate dose of rabies immunoglobulin and the first dose of vaccine, and then complete the series by receiving four additional doses of vaccine on days 3, 7, 14, and 28 after the first dose. Commercially available rabies vaccines are prepared in cell cultures from the inactivated classical rabies virus, i.e. genotype 1. In central Europe, post-exposure treatment is usually given on days 0, 7 and 21; two doses are given on day 0 in the deltoids of both arms and additional doses are given on days 7 and 21. This is one of the WHO validated vaccination schedule [24]. In the United Kingdom, pre-exposure vaccination of all bat handlers, as well as post-exposure vaccination of anyone bitten or in other close contacts with bats, are recommended [24].

Some European countries already have immunisation programmes against bat rabies to protect bat handlers, as well as the general population. Pre-exposure vaccination consists of four doses of modern rabies vaccines given at 0, 7 and 21 days [24,25]. Post-exposure prophylaxis should always be considered, no matter how trivial seeming the exposure.

Current tissue cell rabies vaccines and specific immunoglobulins are used against all genotypes of lyssavirus genus. Rabies researchers generally agree that current vaccines confer a protective immune response against different genotypes of lyssaviruses, with the notable exception of West Caucasian bat virus. Antibody response of ≥ 0.5 IU/ml in sera, measuring neutralising antibodies of vaccinated subjects, is admitted as a sufficient antibody level for protection [25].

Underreporting of cases?

European bat lyssaviruses are recognised in Europe in a limited number of countries, and in under one third of native bat species. In many countries, there is no research, monitoring or surveillance in this field. Data is limited to accurately mapping the geographical distribution of lyssaviruses in the different bat species across Europe. Over the past fifty years, only about 800 cases of rabid bats have been notified in Europe, and more than 90% of these were in the Netherlands, Denmark, Germany, Poland, Spain and France. Serological examination of carriers of lyssaviruses in living bat populations is interesting for bat researchers and public heath officers. Bats may be seropositive for antibodies against lyssaviruses and yet not be carriers of the virus. Further research on EBLV viruses occurring in bat infections and different animal species across Europe will be welcomed. At the same time laboratory confirmation of viral encephalitis in humans in Europe should include examination on

Table 3

WHO recommendations for treatment according to category-I to category-III exposures

Nature of exposure	Status of biting animals		Recommended treatment
	Exposure	15th day following exposure	
I. Contact but no lesions	Rabid		None
II. Skin licked by bat; scratches or abrasions; minor bites covered	Suspected to be rabid	Healthy	None
		Rabid	Vaccination and administration of rabies immunoglobulins
	Rabid; wild animals or animals unavailable for observations		Vaccine and rabies immunoglobulins immediately according to country by country risk and previous vaccination status
III. Mucosa licked by bat; major bites (multiple or on face, head, finger or neck)	Suspected or rabid domestic or wild animal or animal unavailable for observation		Vaccine and rabies immunoglobulines

Source: From the Eighth Report of the WHO Expert Committee on Rabies. Geneva: World Health Organisation; 1992. WHO Technical Report No.824

lyssaviruses to find out the real risk for domestic human rabies infections. Underreporting of viral encephalitis cases and reporting without the association of an aetiological agent for the disease is well known [26].

Infection with EBLV has been naturally identified in only two other species apart from bats and humans; stone marten and sheep. Most recently Vos et al. [27] reported successful laboratory induced infections of ferrets and mice by EBLV-1 and EBLV-2.

According to the results of studies performed on different bat species in Europe, laboratory testing on the European bat lyssavirus 1 (EBLV-1) was positive in *Tadarida teniotis*, *Myotis myotis* (EBLV-1b), *Myotis nattereri* (EBLV-1b), *Pipistrellus nathusii*, *Vespertilio murinus* (EBLV-1a), *Nyctalus noctula*, *Miniopterus schreibersii* (EBLV-1b) and *Rhinolophus ferrumequinum* (EBLV-1b). However, no virus strain was isolated in this study, and only positive serology and PCR tests were obtained. Infection is not usually lethal for bats [28].

Successful treatment

Rabies pre-exposure vaccination and post-exposure treatment with modern rabies vaccines is safe and protective and should be extended. Although vaccination schedules are well adapted for genotype 1 classical rabies virus, this is not the case for the other genotypes. Despite a lack of evidence, vaccination schedules are still strongly recommended for the other lyssavirus genotypes. In persons occupationally exposed to bats, pre-exposure vaccination is necessary, but for the general population, only post-exposure treatments after bat bites is recommended. Different schedules with different modern generations of rabies cell culture vaccines are approved in Europe, most of all prepared on human diploid cell (HDCV) and chick embryo cell cultures (PCEP).

There have been infrequently deaths reported following bat bites of bat handlers in Europe where EBVL-infected bats reside. Nevertheless, even one case that carries a risk deserves attention of public health. Most bat bites are superficial and do not break through the skin to reach the nerves. Bat researchers use protective plasters and gloves to protect their fingers and hands, or perform disinfection of the wound immediately after bat bites.

Conclusion

Rabies in bats is often considered not to be a serious risk to public health when compared with other threats [29] that may cause higher numbers of human infections per year or are more easily transmissible. No one should handle diseased or dead bats without protection, such as gloves or sticking plaster. Pre-exposure vaccination is also necessary in this context. It is vital to obtain laboratory confirmation of rabies in bat after human exposure through biting incidents. Rabies post-exposure treatment is recommended after bat bites in patients, if previous pre-exposure vaccination was (as usually) not performed.

Significant evidence of positive cases of rabies in European bats in almost all the countries where laboratory confirmation of bat rabies is implemented, and the fact that bats migrate long distances across Europe [30] deserve attention. Health education and information on bat rabies for health workers in various fields and for the public in Europe should be promoted.

According to our experience with travellers, dogs represent a more serious threat in many countries, yet the risk of bat bites also exist. Education and recommendations should be given to travellers in order to reduce their risk of infection [31]. Post-exposure rabies treatment should be recommended to travellers reporting bat bites after returning from countries where bat rabies is confirmed, or where epidemiological data on bat rabies is missing. Experiences worldwide show that modern rabies vaccines are extremely efficient for pre-exposure vaccination and post-exposure treatment of rabies. Vaccines are highly immunogenic, safe and protective [32].

Of 1727 bats examined in Europe in 2003, there were 33 cases of rabies: 0/1204 in England, 2/153 in France, 7/125 in Netherlands, 3/40 in Denmark, 13/73 in Germany, 0/6 in Check Republic, 0/1 in Austria, 0/24 in Switzerland, 0/3 in Hungary, 0/5 in Slovakia, 6/6 in Poland, 1/12 in Ukraine, 1/1 in Russian Federation and 0/74 in Albania [33]. Great caution is needed in interpreting this data, because species should be properly identified, the reason for data submission known, and the virus strains typed. It is certainly not possible to deduce any prevalence figure from this data.

Some countries do not report cases of rabies in bats to the WHO because they do not carry out research in that field. The risk of rabies infection after human contact with bats or bat bites in Europe is obviously present. Pre-exposure rabies treatment is recommended for all those who are occupationally exposed to bats anywhere in the world and in Europe.

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ORIGINAL ARTICLES

Surveillance report

FOX RABIES IN FRANCE

B Toma

Fox rabies was first recorded in France in March 1968, and remained a problem until 1998. In the course of the first two decades and despite the control measures applied, rabies expanded both in terms of the enzootic surface area and number of cases.

The measures applied consisted of actions aimed at reducing fox population density, the mandatory vaccination of domestic carnivores in the officially infected areas, and use of human prophylaxis.

Following the large scale implementation of oral vaccination of foxes, starting 1989-1990, the rabies front was pushed back and yearly incidence decreased until rabies was eliminated at the end of 1998. The comparison of results obtained during both periods of applying various strategies is spectacular. France remains exposed to the risk from bat rabies on one hand, and from accidental cases of canine rabies imported from enzootic countries, on the other.

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Key Words: fox, France, rabies, vaccination

The period between March 1968 and December 1998 represented three decades of fox rabies in France. Looking back over several years, it is possible to evoke the characteristics of the descriptive epidemiology (evolution in time and space) of this fox rabies 'invasion', and the measures applied to control it. After two decades of semi-failures, those measures eventually were successful thanks to the prophylactic 'revolution' represented by oral vaccination of foxes against rabies [1].

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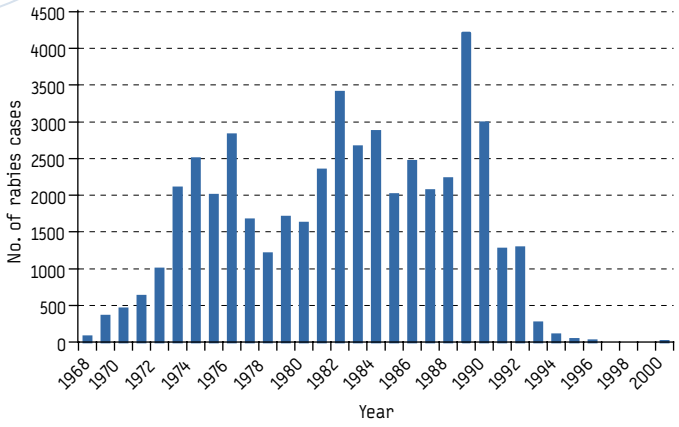
Descriptive epidemiology of fox rabies in France (1968-1998)

The evolution of the yearly incidence of fox rabies in France is shown in figure 1.

FIGURE 1

Evolution of yearly incidence of fox rabies in France, 1968-1998



Source: Bulletin épidémiologique mensuel de la rage en France, 1968-1998 [2]

The evolution of the fox rabies front during the years when the enzootics progressed (1968-1990) is shown in figure 2 [3].